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At page 1, top, delete " EXTENDED RHODAMINE COMPOUNDS USEFUL AS  
FLUORESCENT LABELS", and insert therefor - NUCLEIC ACIDS LABELLED  
A1 WITH EXTENDED RHODAMINE DYES --

At page 1, after the title, please insert: - This application is a division of Application No.  
A2 09/325,243, filed June 3, 1999, which is incorporated herein by reference.--

In the claims:

Please add new claims 46-75.

Please cancel claims 1-45 without prejudice.

*Subj* -- 46. A labelled nucleic acid compound having the formula:

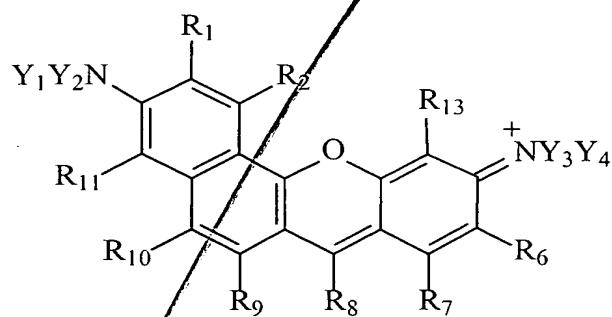
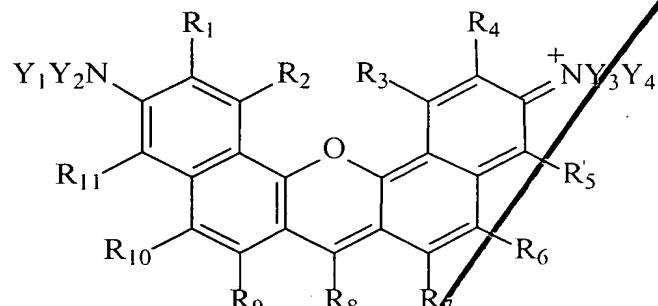
NUC—L—D

wherein

NUC is a nucleic acid compound selected from a nucleoside, a nucleotide, a polynucleotide and analogs thereof;

L is a linkage; wherein if NUC comprises a purine base, the linkage is attached to the 8-position of the purine, if NUC comprises a 7-deazapurine base, the linkage is attached to the 7-position of the 7-deazapurine, and if NUC comprises a pyrimidine base, the linkage is attached to the 5-position of the pyrimidine; and

D is an extended rhodamine dye comprising the structures:



*B1  
Cont*

~~106020 106030 106040~~

wherein

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>9</sub>, R<sub>10</sub>, R<sub>11</sub>, and R<sub>13</sub> when taken alone are selected from -H, alkyl, alkyl independently substituted with one or more Z<sub>1</sub>, heteroalkyl, heteroalkyl independently substituted with one or more Z<sub>1</sub>, aryl, aryl independently substituted with one or more Z<sub>1</sub>, heteroaryl, heteroaryl independently substituted with one or more Z<sub>1</sub>, arylalkyl, arylalkyl independently substituted with one or more Z<sub>1</sub>, heteroarylalkyl, heteroarylalkyl independently substituted with one or more Z<sub>1</sub>, halogen, -OS(O)<sub>2</sub>OR, -S(O)<sub>2</sub>OR, -S(O)<sub>2</sub>NR, -S(O)R, -OP(O)O<sub>2</sub>RR, -P(O)O<sub>2</sub>RR, -C(O)O R, -NR<sub>2</sub>, -NR<sub>3</sub>, -NC(O)R, -C(O)R, -C(O)NR<sub>2</sub>, -CN, and -OR, wherein R is independently selected from -H, alkyl, heteroalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl and linking group; or

R<sub>1</sub> taken together with R<sub>2</sub>, Y<sub>1</sub>, or Y<sub>2</sub>; or

R<sub>4</sub> taken together with R<sub>3</sub>, Y<sub>3</sub>, or Y<sub>4</sub>; or

R<sub>5</sub> taken together with R<sub>6</sub>, Y<sub>3</sub>, or Y<sub>4</sub>; or

R<sub>6</sub> taken together with R<sub>7</sub>, Y<sub>3</sub>, or Y<sub>4</sub>; or

R<sub>10</sub> taken together with R<sub>9</sub> or R<sub>11</sub>; or

R<sub>11</sub> taken together with Y<sub>1</sub>, or Y<sub>2</sub>; or

$R_{13}$  taken together with  $Y_3$  or  $Y_4$   
are selected from alkylene, alkylene independently substituted with one or more  $Z_1$ ,  
heteroalkylene, heteroalkylene independently substituted with one or more  $Z_1$ , arylene,  
arylene independently substituted with one or more  $Z_1$ , heteroarylene, and heteroarylene  
independently substituted with one or more  $Z_1$ ;

$R_8$  is selected from  $-H$ , alkyl, alkyl independently substituted with one or more  $Z_1$ , heteroalkyl, heteroalkyl independently substituted with one or more  $Z_1$ , aryl, aryl independently substituted with one or more  $Z_1$ , heteroaryl, heteroaryl independently substituted with one or more  $Z_1$ , arylalkyl, arylalkyl independently substituted with one or more  $Z_1$ , heteroarylalkyl, and heteroarylalkyl independently substituted with one or more  $Z_1$ ;

Y<sub>1</sub>, Y<sub>2</sub>, Y<sub>3</sub>, Y<sub>4</sub> when taken alone are selected from -H, alkyl, alkyl independently substituted with one or more Z<sub>1</sub>, heteroalkyl, heteroalkyl independently substituted with one or more Z<sub>1</sub>, aryl, aryl independently substituted with one or more Z<sub>1</sub>, heteroaryl, heteroaryl independently substituted with one or more Z<sub>1</sub>, arylalkyl, arylalkyl independently substituted with one or more Z<sub>1</sub>, heteroarylalkyl, and heteroarylalkyl independently substituted with one or more Z<sub>1</sub>; or

$Y_1$  taken together with  $R_1$ ,  $R_{11}$  or  $Y_2$ ; or

$Y_2$  taken together with  $R_1$ ,  $R_{11}$ , or  $Y_1$ ; or

$Y_3$  taken together with  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_{13}$  or  $Y_4$ ; or

$Y_4$  taken together with  $R_4, R_5, R_6, R_{13}$  or  $Y_3$

are selected from alkylene, alkylene independently substituted with one or more  $Z_1$ , heteroalkylene, heteroalkylene independently substituted with one or more  $Z_1$ , arylene, arylene independently substituted with one or more  $Z_1$ , heteroarylene, and heteroarylene independently substituted with one or more  $Z_1$ ; and

$Z_1$  is selected from  $-R$ , halogen,  $-OS(O)_2OR$ ,  $-SO_2OR$ ,  $-SO_2R$ ,  $-SO_2NR$ ,  $-S(O)R$ ,  $-OP(O)O_2RR$ ,  $-P(O)O_2RR$ ,  $-CO_2R$ ,  $-NR_2$ ,  $-NR_3$ ,  $-NC(O)R$ ,  $-C(O)R$ ,  $-C(O)NR_2$ ,  $-CN$ ,  $-O$  and  $-OR$ , wherein  $R$  is independently selected from  $-H$ , alkyl, heteroalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl and linking group.

47. The labelled nucleic acid compound of claim 46 wherein

*A3*

$Y_1$  is taken together with  $R_1$  or  $R_{11}$  and is  $C_2$  or  $C_3$  alkylene or alkylene independently substituted with one or more  $Z_1$ ; or

$Y_2$  is taken together with  $R_1$  or  $R_{11}$  and is  $C_2$  or  $C_3$  alkylene or alkylene independently substituted with one or more  $Z_1$ ; or

$Y_3$  is taken together with  $R_4$  or  $R_5$  or  $R_6$  or  $R_{13}$  and is  $C_2$  or  $C_3$  alkylene or alkylene independently substituted with one or more  $Z_1$ ; or

$Y_4$  is taken together with  $R_4$  or  $R_5$  or  $R_6$  or  $R_{13}$  and is  $C_2$  or  $C_3$  alkylene or alkylene independently substituted with one or more  $Z_1$ .

*Sub 3*

48. The labelled nucleic acid compound of claim 47 wherein the  $C_2$  or  $C_3$  substituted alkylene is gem disubstituted with  $C_1$ - $C_3$  alkyl.

49. The labelled nucleic acid compound of claim 47 wherein the  $C_2$  or  $C_3$  substituted alkylene is gem disubstituted with methyl.

*Sub 3*

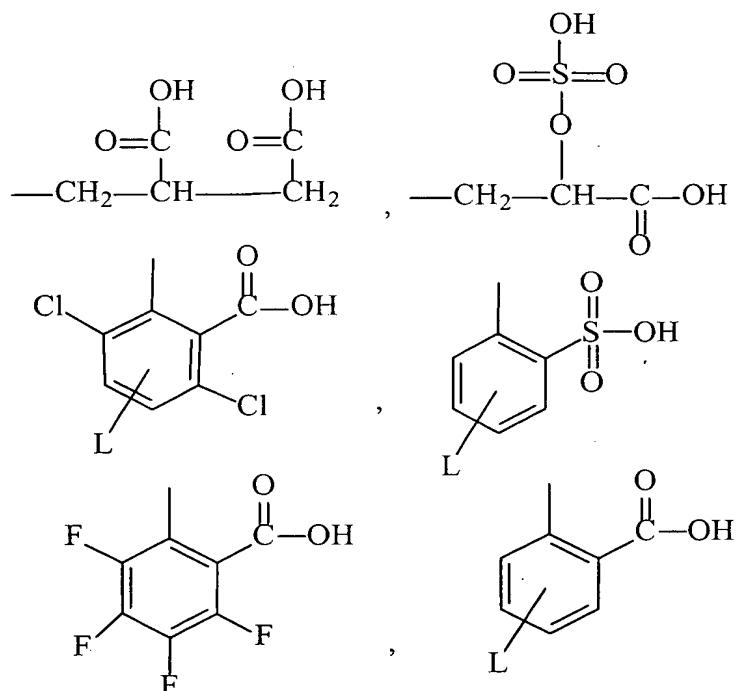
50. The labelled nucleic acid compound of claim 46 wherein  $R_8$  is alkyl independently substituted with one or more substituents selected from halogen, — $C(O)R$ , and — $S(O)_2R$  wherein R is independently selected from —OH, O-alkyl, - $NH_2$ , N-alkyl and a linkage.

51. The labelled nucleic acid compound of claim 46 wherein  $R_8$  is — $CF_3$ .

52. The labelled nucleic acid compound of claim 46 wherein  $R_8$  is aryl or aryl independently substituted with one or more  $Z_1$ .

*Sub 3*

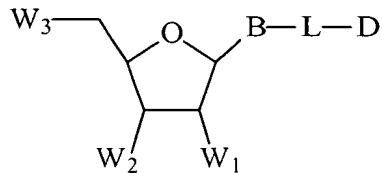
53. The labelled nucleic acid compound of claim 46 wherein  $R_8$  is selected from the structures:



wherein L is a linkage.

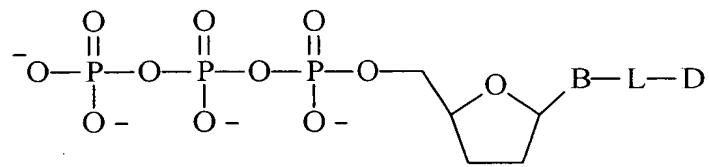
54. The labelled nucleic acid compound of claim 46 wherein NUC comprises a nucleobase selected from uracil, cytosine, deazaadenine, and deazaguanosine.

55. The labelled nucleic acid compound of claim 46 having the structure:



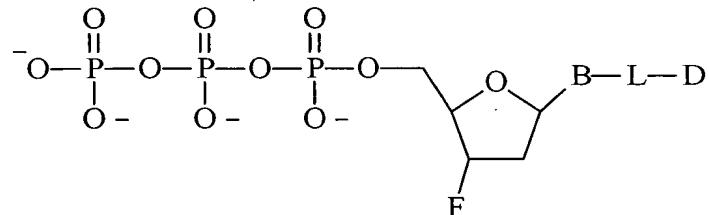
wherein B is a nucleobase; W<sub>1</sub> and W<sub>2</sub> taken separately are selected from -H, -OH, and -F; and W<sub>3</sub> is selected from -OH, monophosphate, diphosphate, triphosphate and phosphate analog

56. The labelled nucleic acid compound of claim 46 having the structure:



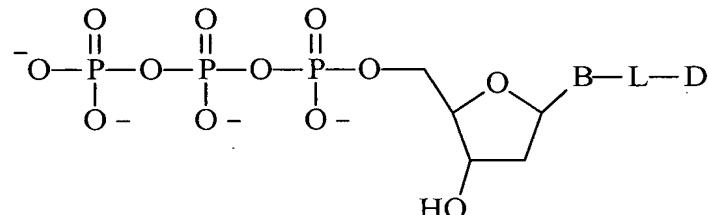
wherein B is a nucleobase.

57. The labelled nucleic acid compound of claim 46 having the structure:



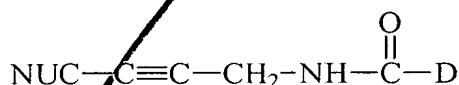
wherein B is a nucleobase.

58. The labelled nucleic acid compound of claim 46 having the structure:

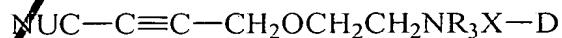


wherein B is a nucleobase.

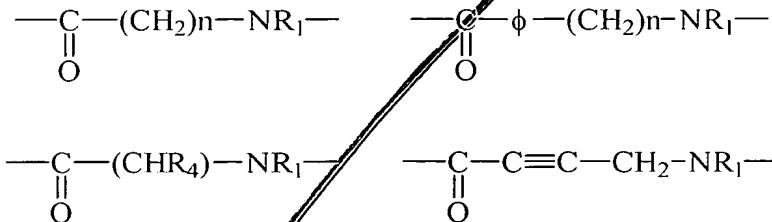
*Sub B1*  
59. The labelled nucleic acid compound of claim 46 wherein L is attached to a nucleobase of NUC and to D in the structure:



60. The labelled nucleic acid compound of claim 46 wherein L is attached to a nucleobase of NUC and to D in the structure:



wherein R<sub>3</sub> is selected from -H and (C<sub>1</sub>-C<sub>6</sub>) alkyl; and X is selected from the structures:



where n ranges from 1 to 5;  $\phi$  is aryldiyl; and R<sub>1</sub> is selected from -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl and protecting group.

61. The labelled nucleic acid compound of claim 46 wherein L is attached at R<sub>8</sub> of D.

62. The labelled nucleic acid compound of claim 46 wherein NUC is a nucleotide and D is a donor dye and an acceptor dye wherein fluorescence energy transfer occurs between the donor dye and acceptor dye and at least one of the donor dye and acceptor dye is an extended rhodamine dye.

63. The labelled nucleic acid compound of claim 46 wherein NUC is a polynucleotide and L is attached to the polynucleotide at a position selected from the 5' terminus, the phosphodiester backbone, a nucleobase, and the 3' terminus.

64. The labelled nucleic acid compound of claim 63 wherein L is an aminohexyl linkage attached to the polynucleotide at the 5' terminus.

65. The labelled nucleic acid compound of claim 46 wherein NUC is a polynucleotide labelled with a donor dye and an acceptor dye wherein fluorescence energy transfer occurs between the donor dye and acceptor dye and at least one of the donor dye and acceptor dye is an extended rhodamine dye.

66. A method of PCR enzymatic synthesis comprising amplifying a template DNA with nucleotide triphosphates, polymerase, and two or more primers wherein the primers are complementary to the template DNA sequence and at least one of the primers is a labelled polynucleotide of claim 63.

67. A method of fragment analysis comprising the steps of:

AB  
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forming one or more labeled polynucleotide fragments, the fragments being labeled with the labelled nucleic acid compound of claim 46;  
resolving the one or more labeled polynucleotide fragments; and  
detecting the resolved labeled polynucleotide fragments.

68. The method of claim 67 wherein the resolving step is an electrophoretic size-dependent separation process and the one or more labeled polynucleotide fragments are detected by fluorescence.

69. A kit for PCR enzymatic synthesis comprising one or more nucleotide triphosphates, polymerase, and two or more primers wherein one or more of the nucleotide triphosphates is a labelled nucleic acid compound according to claim 58.

70. A kit for PCR enzymatic synthesis comprising one or more nucleotide triphosphates, polymerase, and two or more primers wherein at least one of the primers is a labelled polynucleotide of claim 63.

71. A kit for fragment analysis comprising one or more nucleotide triphosphates, a chain-terminating nucleotide analog and a primer, wherein one or more of the nucleotide triphosphates is a labelled nucleic acid compound according to claim 55.

72. A kit for fragment analysis comprising one or more nucleotide triphosphates, a chain-terminating nucleotide analog and a primer, wherein one or more of the nucleotide triphosphates is a labelled nucleic acid compound according to claim 58.

73. A kit for fragment analysis comprising one or more nucleotide triphosphates, a chain-terminating nucleotide analog and a primer, wherein said chain-terminating nucleotide analog is a labelled nucleic acid compound according to claim 56.

74. A kit for fragment analysis comprising one or more nucleotide triphosphates, a chain-terminating nucleotide analog and a primer, wherein said chain-terminating nucleotide analog is a labelled nucleic acid compound according to claim 57.